REMARKS/ARGUMENTS

I. Status of the Claims

Upon entry of this Amendment, claims 97-100, 103, 104, 130, 131, 195-198, 220, 233, 235, 243 and 245-261 are pending. Claims 91-95, 132-180 and 183-192 have been cancelled subsequent to their withdrawal from examination by the Examiner as being drawn to non-elected subject matter. All amendments to and cancellation of claims are made without prejudice or disclaimer of any cancelled subject matter. Applicants reserve the right to pursue all cancelled subject matter in one or more divisional and/or continuation applications.

Claims 97-100, 103,104, 130, 131, 195-198, 220, 233, 235 and 243 have been amended. Claims 245-261 have been added. Support for the amended and new claims is found throughout the application as filed, e.g., in the originally-filed claims and throughout the specification, e.g., page 17, lines 20-23 (forms of the allergen component), page 23, lines 6-9 ("effective dose of an allergen for desensitization"), page 31, lines 21-22 (about 65-17,600 BAU/dosage form), page 33, line 3 (allergen extract content of about 0.5 μg – 5 mg/dosage form), page 33, lines, 20-22 (major allergen content of about 0.05 μg – 500 μg/dosage form), page 39, lines 11-12 (matrix comprising starch or gelatine), page 40, lines 1-2 (matrix comprising mannitol), page 55, line 10 through page 56, line 10 (multidose containers, e.g., blister packs, dosing regimens that lack an up-dosing step, treatment pack for treatment of allergy or alleviating symptoms of allergy), and page 56, lines 11-17 (kit comprising treatment pack and instructions or information "of value to the user").

By this Amendment, no new matter has been added to the application.

II. Response to Rejection Under 35 U.S.C. §103(a)

Claims 97-104, 130, 131, 193-198, 203-205, 213-244 were rejected as being allegedly obvious over WO 00161 117 ("WO '117") in view of Roser et al., U.S. Patent No. 5,762,961 ("Roser"); Cho et al., *Dissertation Abstracts Int'l*, (1993) 54:1940, STN 19930920 ("Cho");

Linter, Chapter 82, pp. 1478-1484 in *Remington's Pharmaceutical Sciences*, 17th edition (1985) ("Remington's"); Cleland et al., *J. Pharm. Sci.*, (2001) 90:310-321 ("Cleland"); Pradalier et al., *Allergy*, (1999) 54:819-828 ("Pradalier"), and; Hordijk et al., *Allergol. Immunopathol (Madr)*, (1998), 26:234-40 ("Hordijk"). The rejection is traversed as it applies to the subsisting claims. The cited references fail, individually or collectively, to suggest the single phase allergy vaccine system for treatment of allergy or for alleviating allergy symptoms in a subject of claims 97-100, 103,104, 130, 131, 195-198, 220, 233, 235 and 243, the vaccine kit for desensitizing a subject to an allergen without an up-dosing period of claims 245-260, or the single phase, up-dosing free dosage kit for self administration of an anti-allergen, desensitization therapy of claim 261. The rejection should therefore be withdrawn.

The Examiner's attention is first directed to claim 97 which claims a single phase allergy vaccine system for treatment of allergy or for alleviating allergy symptoms. Allergy vaccine systems typically include an up-dosing component consisting of increasing dosages of allergen and a maintenance component. The allergy vaccine system of claim 97 comprises a plurality of dosage forms that are "substantially identical" and comprise "an even dose" of allergen. Claim 97 thus excludes an up-dosing component. Similarly, claim 245 is directed to a "vaccine kit for desensitizing a subject to an allergen without an up-dosing period" and which comprises "a plurality of separate compartments comprising substantially identical... unit dosage forms ... comprising an even dose [of allergen] in an amount effective to induce an allergen specific immune response... without up-dosing." Each of the other subsisting claims depend either directly or indirectly from either claim 97 or 245 and are thus also each directed to a vaccine system or kit that excludes an up-dosing component. The updosing-free dosage kit for self administration of claim 261 similarly comprises a plurality of doses, each "comprising a substantially identical dose of an allergen in an amount effective for inducing an immune response."

The presently claimed vaccine systems and kits are thus not maintenance dosage systems or kits. They are complete allergy vaccine systems and kits that explicitly do not require up-dosing. The inclusion of an up-dosing component would change the salient characteristics of the

claimed vaccine systems and kits. This feature thus cannot be ignored. "[O]bviousness requires a suggestion of all limitations in a claim." *CFMT, Inc.,v. Yieldup Int'l Corp.,* 349 F.3d 1333 (Fed. Cir. 2003), *citing In re Royko,* 490 F.2d 981, 985. This is important because the claimed vaccine systems and kits are non-obvious for what they do not include as well as for what they include. Notwithstanding the lack of up-dosing dosage forms in the claimed vaccine systems and kits, the substantially identical, even-dose dosage forms present in the vaccine systems and kits are "effective for inducing an immune response specific to said allergen in said subject, to treat said allergy or alleviate said allergy symptoms in said subject" (*see* claim 97), "effective to induce an allergen specific immune response to said allergen in said subject" (*see* claim 245), or "effective for inducing an immune response specific to said allergen in said subject" (*see* claim 261).

The combination of a single, even dose in all of the dosage forms in the claimed vaccine systems or kits, the absence of dosage forms with up-dosing amounts is not suggested in the cited prior art, taken individually or collectively. The elimination of up-dosing was contrary to the conventional wisdom. Prior to the present invention, conventional wisdom held that attempting allergy therapy with an effective even-dose of therapy would have possibly fatal complications. The claimed vaccine systems for treatment of allergy or for alleviating allergy symptoms and kits for use in desensitizing a patient to an allergen thus run counter to the state of the art when the application was filed. This is strong evidence that the claims are not obvious.

The instant specification thus describes that allergy vaccination was not widely used because the course of vaccination is long and there is a risk of allergic side reactions. Specification, page 6, lines 1-5. Ordinary vaccinations against infectious agents use single or a few high dose immunizations. Specification, page 6, lines 5-6. However, this regimen cannot be used for allergy vaccination since a pathological immune response is already ongoing. Specification, page 6, lines 6-8.

Conventional allergy vaccination is carried out with multiple subcutaneous immunizations over a period of time. The course of treatment is two-phased – an up-dosing phase and a maintenance phase. Specification, page 6, lines 9-11. The up-dosing phase consists

of increasing, i.e., not constant or the same doses applied over typically a 16 week period. The initial doses in the up-dosing phase are minute. When the maintenance dose is reached at the end of up-dosing, the final dose is applied for the maintenance period typically with injections every six weeks. Specification, page 6, lines 11-15. The patient must remain under emergency-prepared medical supervision after each dose in case of anaphylactic side reactions. Specification, page 6, lines 15-18. Attempts to improve allergy vaccinations have ranged from modification of the allergen to changing the route of administration. Specification, page 6, lines 23-26. Each has drawbacks. *See* Specification, page 7, line 3 through page 9, line 21.

The presently-claimed vaccine systems and kits overcome many of the obstacles associated with conventional allergy vaccination via injection or prior compositions for use in prior methods of oromucosal allergy vaccination. The claimed vaccine systems and kits, are sufficiently stable, safe, effective, and simple to use that they may packaged into kits for self administration by an allergy patient over the course of allergen therapy. The vaccine systems and kits that are disclosed in the specification and presently claimed have, in fact, been tested in clinical tests wherein allergy patients successfully performed anti-allergen therapy by unsupervised, daily, self-administration of the unit dosage forms of the present claims at home over an average period of 22 months. *See* Rak et al. (Abstract 656), Kapp et al. (Abstract 658), and Emminger et al. (Abstract 663) in *Allergy* 62 (Suppl. 83) at pages 237, 238 and 240, respectively (respectively, Non-Patent Literature (NPL) documents 5-7 in an Information Disclosure Statement (IDS) submitted herewith). Subsequent, follow-up studies confirmed the safety and efficacy of the anti-allergy therapy. See Dahl et al., *J. Allergy Clin. Immunol.* 2006, 118:434-440 and Durham et al., *J. Allergy Clin. Immunol.* 2010, 125:131-138 (NPL documents 1 and 2 in the attached IDS).. In short, the claimed solid, single phase vaccine systems and kits are so far superior to prior art formulations that they are suitable for use in methods of allergen therapy that were unobtainable before the filing the of the present application. This is further strong evidence that the claimed vaccine systems and kits are not obvious over the prior art of record.

For at least the reasons set out above, the instant rejection should be withdrawn.

The rejection should additionally be withdrawn because the Examiner has failed to set out a valid rationale for combining the prior art to arrive at the instant claims.

The Examiner cites WO '117 as disclosing a fast-dispersing dosage form comprising a carrier containing fish gelatin and active ingredient, which disintegrates or disperses within, e.g., 1-60 sec after being placed in the oral cavity. According to the Examiner, the dosage form can be a solid dosage form prepared from a mold and can contain certain other non-active materials and active ingredients. The Examiner refers to dosage forms containing fish gelatin and mannitol formed in pre-formed blister pockets. The Examiner refers to Roser as disclosing rapidly soluble tablets containing other excipients and active ingredients. Cho is added as disclosing that addition of mannitol stabilized protein against conformational changes in the presence of adjuvants such as aluminum oxyhydroxide or aluminum phosphate. Remington's is added as disclosing that although there are exceptions, 90% of labeled potency is generally recognized as the minimum acceptable potency level and that physical factors such as heat and moisture can initiate or accelerate chemical reactions. Cleland is cited as disclosing that proteins are often dried to reduce the rate of chemical and physical degradation and that sugars can stabilize proteins during lyophilization and storage. The Examiner cites to Pradalier for the proposition that sublingual tablets are safe and easier to use for immunotherapy of seasonal rhinoconjunctivitis, asthma, and perennial rhinitis and to Hordijk as disclosing that patients given 9500 BU of grass pollen extract sublingually had a reduction in the severity of allergic complaints.

The Examiner's combining of the cited prior art is not well taken, as it combines bits and pieces of the cited references to arrive at the instant claims, while failing to consider differences among the references and between the references and the claimed invention that would lead one of ordinary skill in the art to conclude that the references collectively do not suggest the claimed invention.

The Examiner need look no farther than WO '117 and Roser to see that the combination of cited references is forced and overreaching. All of the examples and the preferred embodiment of WO '117 are concerned solely with a "solid fast-dispersing dosage form

containing a network of active ingredient and a water soluble or water-dispersible carrier comprising fish gelatin." *See* WO '117 at page 7. Such dosage forms are formed by freeze-drying. *See* WO '117 at page 8 and Examples. Roser is directed solely to RS (rapidly soluble) tablets obtained by formulating a volatile salt with dry components in powder form and compressing into tablets. Roser's dry-formulated compositions are thus fundamentally different from the fast-dispersing dosage forms prepared by freeze-drying that are taught by WO '117. Roser's disclosure that the disclosed dry-formulated compositions may include components, such as certain binders, and active components such as proteins, natural peptides or antigens thus does not suggest that such components should or could be formulated in a very different dosage-form, as disclosed in WO '117. None of the other references cited by the Examiner contain any information that would cure the incompatibility between Roser and WO '117. It is thus improper for the Examiner to combine WO '117 and Roser to arrive at the instant claims. The rejection of each of the claims relies on the combination of WO '117 and Roser. For at least this reason, the instant rejection should be withdrawn in its entirety.

The Examiner overreaches again in combining the prior art to arrive at dosage forms for use in even-dosed allergen treatments that do not require up-dosing. WO '117 does not discuss the ability to eliminate up-dosing in allergy vaccines, or discuss constant-dose allergy vaccines, which, as discussed at length above, are important features of the present claims. Rather, WO '117 is primarily directed to fish gelatin matrices. One of ordinary skill in the art would have used conventional vaccination kits on patients needing an allergy vaccine as explained above and in the present specification.

None of the Examiner's secondary references cure these defects in WO '117; each secondary reference is similarly deficient. Only Pradalier and Hordijk discuss allergy vaccinations in any detail, and these references are concerned with conventional allergy vaccines. Pradalier discloses a "progression of doses phase" and "a 15-day progression of dose phase," i.e., up-dosing. Pradalier at pages 819 and 821. Hordijk discloses a study with "an incremental phase of approximately 3 weeks" followed by a coseasonal maintenance phase." Hordijk at page 2. Pradalier and Hordijk thus disclose, conventional allergy vaccines, not the

claimed vaccine systems and kits. For this additional reason, the prior art cited by the Examiner and the instant rejection should be withdrawn.

Additionally, with respect to claims directed to non-compressed (*see* claims 103 and 247) and lyophilized (*see* claims 104 and 248) dosage forms, the Examiner, paints the teachings of Pradalier much too broadly. The Examiner thus asserts that Pradalier discloses sublingual tablets for administration of allergens and "As such, solid oral mucosal dosage forms to administer allergens are suggested by the art." Final Office Action at page 7, bottom. The claimed, non-compressed and lyophilized dosage forms, however, are not directed to tablets and Pradalier's teachings concerning tablets cannot be extended to such dosage forms. For this reason additionally, the prior art of record does not suggest claims 103, 104, 247 and 248, and thus for this reason additionally the rejection of these claims should be withdrawn.

Additionally, the instant rejection should be withdrawn because the claimed invention has unexpected, superior results compared to the closet prior art.

The closest prior art may be considered to be either WO '117, the primary reference cited by the Examiner, or Pradalier, which discloses conventional SLIT therapy. As recognized by the Examiner, neither WO '117 nor Pradalier discloses the claimed invention. Neither does either of WO '117 or Pradalier recognize any benefit of using the claimed vaccine systems and kits. As discussed in greater detail above, the present application sets out the benefits of the claimed invention, namely that it may be used for even-dosage allergen therapy and is so safe and easy to use that patients may effect therapy at home, without supervision by a health professional. None of the prior art of record suggests that the claimed invention would be so safe and easy to use for up-dosing free immunotherapy that it could be safely and effectively used by a patient at home.

The Examiner's failure to give weight to the superior, unexpected results obtained by the claimed invention is not well taken. In judging unexpected results, the claimed invention must be measured against the closest prior art, not against itself. *Pfizer, Inc., v. Apotex, Inc.,* 480 F.3d 1348, 1370 (Fed. Cir. 2007). The Applicant "is not required to compare the claimed invention with subject matter that does not exist in the prior art." *Id., citing in re Geiger,* 815 F.2d 686, 689 (Fed. Cir. 1987) (Newman, J., concurring). Here, the closest prior art cited by the Examiner

may be either WO '117 or Pradalier. The Applicant is not required to show unexpected results compared to the combination of WO '117 and Pradalier. WO '117 fails to disclose any dosage form comprising an allergen. Pradalier gives only general disclosure that allergen is administered in sublingual tablets, but fails to disclose administering allergens in the claimed dosage form. Thus, neither WO '117 nor Pradalier provides a dosage form with the unexpected, superior effects of the claimed dosage form. This is objective evidence that the claimed invention is not obvious over the prior art of record. For this reason additionally, the instant rejection should be withdrawn.

Lastly, in piecing together the prior art to set out the present rejection, the Examiner is using the Applicants' own specification as the basis for combining unrelated prior art teachings in order to reject the claims under the guise of obviousness. This type of hindsight reconstruction has been condemned by the courts. *See Grain Processing Corp. v. American Maize-Products Co.*, 840 F.2d 902, 907 (Fed. Cir. 1988) ("Care must be taken to avoid hindsight reconstruction by using 'the patent in suit as a guide through the maze of prior art references, combining the right references in the right way so as to achieve the result of the claims in suit.'", *quoting Orthopedic Equip. Co. v. United States,* 702 F.2d 1005, 1012 (Fed. Cir. 1983); In re Lee 277 F.3d 1338, 1343 ("It is improper, in determining whether a person of ordinary skill in the art would have been led to this combination of references, simply to '[use] that which the inventor taught against its teacher,'" *quoting W.L. Gore v. Garlock Inc.,* 721 F.2d 1540, 1553 (Fed. Cir. 1983). Here, it is the Applicant and not the prior art that teaches the combination of features called for in the present claims. For this reason additionally, the instant rejection should be withdrawn.

For all of the reasons set out above, the subsisting claims are not obvious over WO '117 in view of Roser, Cho, Remington's, Cleland, Pradalier, and Hordijk. Reconsideration of the claims and withdrawal of all rejections under 35 U.S.C. §103 is requested.

III. Conclusion

This application is in condition for allowance, which is earnestly solicited.

Respectfully submitted,

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